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=> s CTL response
L1 14238 CTL RESPONSE

=> s l1 and injection
L2 1448 L1 AND INJECTION

=> s l2 and lymphnode
L3 1 L2 AND LYMPHNODE

=> d l3 cbib abs

L3 ANSWER 1 OF 1 MEDLINE on STN
79228531 Document Number: 79228531. PubMed ID: 88878. Suppressor cells for in vivo cytotoxic responses--regulation of the in vivo activation of cytotoxic T-lymphocytes by suppressive cells. Droge W; Sussmuth W; Franze R. ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1979) 114 319-25. Journal code: 0121103. ISSN: 0065-2598. Pub. country: United States. Language: English.

AB A significant in vivo activation of cytotoxic T-lymphocytes (CTL) against trinitrophenyl (TNP)-modified autologous cells and of a DNA-synthesis response in the peripheral **lymphnodes** is observed in cyclophosphamide (CyP) treated mice after skinpainting with trinitrochlorbenzene (TNCB) or after **injection** of TNP-coupled spleen cells (TNP-Spl) into the footpads. The activation of these responses can be suppressed by the transfer of spleen cells or **lymphnode** cells from skinpainted normal mice, but not from skinpainted mice that had been pretreated with CyP. Suppressive activity is also induced by **injections** of TNP-Spl i.p. or trinitrobenzosulfonate (TNBS) i.v. Optimal activation of suppression occurs with 3--4 days. The suppressive activity is antigen-specific at least in respect to its activation. Suppressor cells of this kind also suppress the induction of delayed hypersensitivity (DH) responses and the priming for in vitro secondary responses. However, these two responses are less sensitive to the suppression, and their in vivo activation is accordingly much less restricted with the in vivo activation of DNA-synthesis and primary **CTL responses**. DH and CMC memory can be activated ty TNCB skinpainting without pretreatment with CyP.

=> s injection
L4 1599515 INJECTION

=> s l4 and lymph node
L5 19853 L4 AND LYMPH NODE

=> s l5 and tumor
L6 4997 L5 AND TUMOR

=> s l6 and lymphatic injection
L7 3 L6 AND LYMPHATIC INJECTION

=> dup remove l7
PROCESSING COMPLETED FOR L7

L8 3 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs

L8 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
1984:292441 Document No.: BA78:28921. USE OF DIRECT LYMPHO VASCULAR **INJECTION** OF LABELED LIPOSOMES IN THE EVALUATION OF BARRIER FUNCTION OF REGIONAL **LYMPH NODES** IN RABBITS WITH THE BROWN PEARCE CARCINOMA. ISPENKOVA L I. RES. INST. MED. RADIOL., ACAD. MED. SCI. USSR, OBNINSK, USSR.. EKSP ONKOL, (1983) 5 (5), 73-75,79. CODEN: EKSODD. ISSN: 0204-3564. Language: Russian.
AB A direct **lymphatic injection** (DLI) of 125I-liposomes permitted a quantitative estimation of the disturbance in the **lymph node** barrier function from the level of preparation fixation delay in the **lymph node** (LN). In **tumor**-bearing animals [Brown-Pearce carcinoma-bearing rats] the preparation concentration in the **lymph node** was higher than in the intact ones only 3 h after the **injection**. Later, the preparation accumulation in the **tumor** LN was lower than in the intact node. During the aseptic inflammation the preparation concentration in the **lymph node** was lower than in the intact **lymph node** and higher in **tumor**-bearing rabbits. External radiometry data confirm the results obtained. DLI of labeled liposomes may be used for diagnosis and probably for antitumoral preparation transport.

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
1972:10167 Document No. 76:10167 Distribution of Lipiodol F-131I after **lymphatic injection** in the dog. Fava, G.; Bertoli, M. A.; De Vecchi, A.; Giavelli, S.; Invernizzi, A.; Sichirollo, A. E. (Ist. Naz. Stud. Cura Tumori, Milan, Italy). Ateneo Parmense, Acta Bio-Medica, 42(1), 11-21 (Italian) 1971. CODEN: ATPRAN. ISSN: 0004-6531.
AB The body distribution of the X-ray contrast agent, 131I-labeled Lipiodol F, and its changes with time were studied in dogs after lower limb endolymphatic lymphography (4 mCi/dog). Radioactivity was measured both externally and in organ samples after sacrifice. High amts. of radioactive material were found in the **lymph nodes**, lung, and liver, and lower amts. in the other organs tested. The metabolism of Lipiodol is discussed; the use of this radioactive material in lymphography as therapy for some neoplasms of the retroperitoneal **lymph nodes** is considered justified.

L8 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
1971:36262 Document No.: BR07:36262. DISTRIBUTION OF COLLOIDAL RADIO GOLD AND RADIATION DOSE IN **LYMPH NODES** FOLLOWING ENDO **LYMPHATIC INJECTION**. NORVELL S T; FUNG G; CUNNINGHAM R M; LIMAN Z. Clin. Res., (1969) 17 (4), 666. CODEN: CLREAS. ISSN: 0009-9279. Language: Unavailable.

=> s lymph node injection
L9 45 LYMPH NODE INJECTION

=> s l9 and CTL response
L10 0 L9 AND CTL RESPONSE

=> dup remove l9
PROCESSING COMPLETED FOR L9
L11 24 DUP REMOVE L9 (21 DUPLICATES REMOVED)

=> d l11 1-24 cbib abs

L11 ANSWER 1 OF 24 MEDLINE on STN DUPLICATE 1
2003333764 Document Number: 22748538. PubMed ID: 12865998. Popliteal and mesenteric **lymph node injection** with

methylene blue for coloration of the thoracic duct in dogs. Enwiller Tara M; Radlinsky Maryann G; Mason Diane E; Roush James K. (Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS, USA.) VETERINARY SURGERY, (2003 Jul-Aug) 32 (4) 359-64. Journal code: 8113214. ISSN: 0161-3499. Pub. country: United States. Language: English.

AB OBJECTIVE:To describe and compare the time of onset and intensity of thoracic duct coloration after injection of methylene blue into a mesenteric or popliteal lymph node. STUDY DESIGN: Experimental study. ANIMALS: Twenty adult dogs. METHODS: A right tenth intercostal thoracotomy, a right paracostal laparotomy, and an approach to the right popliteal lymph node were performed on each dog. Methylene blue (0.5 mg/kg of a 1% solution, maximum 10 mg) was injected into either a mesenteric (group M, 10 dogs) or popliteal (group P, 10 dogs) lymph node. Thoracic duct color was graded (0 to 3) every 5 minutes for 60 minutes. Statistical analysis was performed on mean thoracic duct color grade data, on number of successful outcomes between groups M and P, and between weight groups. RESULTS: Coloration of the thoracic duct occurred in all group M dogs and 6 group P dogs. Coloration was first recorded 0 to 10 minutes after injection in all dogs and persisted for 60 minutes in 15 dogs. Mean thoracic duct color grade was significantly increased postinjection compared with preinjection at all times in group M. More successful outcomes occurred in group M (P =.03). CONCLUSIONS: Methylene blue injected into mesenteric or popliteal lymph nodes was successful in coloring the thoracic duct, but both mean grade and number of successful outcomes were significantly higher after mesenteric injection. CLINICAL RELEVANCE: Thoracic duct coloration after **lymph node injection** occurred within 10 minutes and persisted for 60 minutes. This information is useful in planning thoracic duct ligation in cases of chylothorax when observation of the duct is desired. Injection of both lymph node sites was successful, but mesenteric node injection was a more reliable technique.

L11 ANSWER 2 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

2003:348465 Document No.: PREV200300348465. Research on preparation of antibody against Schistosomal circulating antigen. Chen Si-li (1); Li Ling; Chen Qiang; Zhuo Yu-si; Chen Si-yi; Wu Feng-jiao; Chen Si-zhi. (1) College of Life Science, Central China Normal University, Wuhan, 430079, China China. Huazhong Shifan Daxue Xuebao (Ziran Kexue Ban), (March 2003, 2003) Vol. 37, No. 1, pp. 87-89. print. ISSN: 1000-1190. Language: Chinese.

AB CAA and CCA are two reliable means of schistosome infection test and therapeutic evaluation. With the different schistosome antigenic components, The experimental rabbits were immunized by different routes and methods. The result showed that microimmunization and intra-popliteal **lymph nodes injection** immunization had satisfactory immune effect. For intra-popliteal **lymph nodes injection** immunization, good immune effect could still be gained even if the antigen was injected around popliteal lymph nodes. The sensitivity to detect CSA of the antiserum, which was from methylating carrier protein immunization in soluble imaginal antigen, enhanced significantly. By adding Freund's complete adjuvant and complex nucleotide sodium to methylating carrier imaginal antigen, the immune success rate was 87.50% and the titer of antiserum was above 1:12 800.

L11 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

2002:443013 Document No. 136:400596 Preparation of anti-staphylokinase IgG for immunoassay of recombinant staphylokinase useful as thrombolytics. Tong, Mingqing; Wang, Shipeng; Tong, Bin (Jinpeng Bio-Technology Co., Ltd., Chengdu, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1316438 A 20011010, 8 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 2000-112826 20000405.

AB Antiserum specific to recombinant staphylokinase is prepd. by immunizing rabbits with water-in-oil emulsion contg. staphylokinase-bovine serum

albumin conjugate and Freund's adjuvant. Anti-staphylokinase IgG is purified by protein G chromatog. column, labeled with enzyme by sodium iodide method, and used for immunodetn. (ELISA) of staphylokinase content in pharmaceutical compns. or patient blood samples.

L11 ANSWER 4 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2

2001384251 EMBASE CD44-dependent lymphoma cell dissemination: A cell surface CD44 variant, rather than standard CD44, supports in vitro lymphoma cell rolling on hyaluronic acid substrate and its in vivo accumulation in the peripheral lymph nodes. Wallach-Dayan S.B.; Grabovsky V.; Moll J.; Sleeman J.; Herrlich P.; Alon R.; Naor D.. D. Naor, Lautenberg Ctr. Gen./Tumor Immunol., The Hebrew Univ.-Hadassah Med. Sch., Jerusalem 91120, Israel. naord@md2.huji.ac.il. Journal of Cell Science 114/19 (3463-3477) 2001. Refs: 74.
ISSN: 0021-9533. CODEN: JNCSAI. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Cell motility is an essential element of tumor dissemination, allowing organ infiltration by cancer cells. Using mouse LB lymphoma cells transfected with standard CD44 (CD44s) cDNA (LB-TRs cells) or with the alternatively spliced CD44 variant CD44v4-v10 (CD44v) cDNA (LB-TRv cells), we explored their CD44-dependent cell migration. LB-TRv cells, but not LB-TRs or parental LB cells, bound soluble hyaluronic acid (HA) and other glycosaminoglycans (GAGs), and exclusively formed, under physiological shear force, rolling attachments on HA substrate. Furthermore, LB-TRv cells, but not LB-TRs cells or their parental LB cells, displayed accelerated local tumor formation and enhanced accumulation in the peripheral lymph nodes after s.c. inoculation. The aggressive metastatic behavior of i.v.-injected LB-TRV cells, when compared with that of other LB-transfectants, is attributed to more efficient migration to the lymph nodes, rather than to local growth in the **lymph node**. **Injection** of anti-CD44 monoclonal antibody or of the enzyme hyaluronidase also prevented tumor growth in lymph nodes of BALB/c mice inoculated with LB-TRv cells. The enhanced in vitro rolling and enhanced in vivo local tumor growth and lymph node invasion disappeared in LB cells transfected with CD44v cDNA bearing a point mutation at the HA binding site, located at the distal end of the molecule constant region. These findings show that the interaction of cell surface CD44v with HA promotes cell migration both in vitro and in vivo, and they contribute to our understanding of the mechanism of cell trafficking, including tumor spread.

L11 ANSWER 5 OF 24 MEDLINE on STN DUPLICATE 3

2001126922 Document Number: 21079786. PubMed ID: 11212262. Intranodal immunization with tumor lysate-pulsed dendritic cells enhances protective antitumor immunity. Lambert L A; Gibson G R; Maloney M; Durell B; Noelle R J; Barth R J Jr. (Department of Surgery, Dartmouth Medical School and Norris Cotton Cancer Center, Lebanon, New Hampshire 03756, USA.) CANCER RESEARCH, (2001 Jan 15) 61 (2) 641-6. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB We developed a technique for direct inguinal **lymph node injection** in mice to compare various routes of immunization with tumor lysate-pulsed dendritic cell (DC) vaccines. Syngeneic, bone marrow-derived, tumor lysate-pulsed DCs administered intranodally generated more potent protective antitumor immunity than s.c. or i.v. DC immunizations. Intranodal immunization with ovalbumin peptide-pulsed DCs induced significantly greater antigen-specific T-lymphocyte expansion in the spleen than either s.c. or i.v. immunization. Furthermore, a significantly more potent, antigen-specific TH1-type response to the ovalbumin peptide was induced by intranodal, compared with s.c. or i.v., immunization. Intranodal immunization, designed to enhance DC-T cell interaction in a lymphoid environment, optimizes induction of T lymphocyte-mediated protective antitumor immunity. These results support the use of intranodal immunization as a feasible and effective route of DC vaccine administration.

L11 ANSWER 6 OF 24 MEDLINE on STN DUPLICATE 4

1999189817 Document Number: 99189817. PubMed ID: 10089947. Number and anatomical extent of lymph node metastases in gastric cancer: analysis using intra-**lymph node injection** of activated carbon particles (CH40). Okamoto K; Sawai K; Minato H; Yada H; Shirasu M; Sakakura C; Otsuji E; Kitamura K; Taniguchi H; Hagiwara A; Yamaguchi T; Takahashi T. (First Department of Surgery, Kyoto Prefectural University of Medicine, Japan.. okamoto@1surg.kpu-m.ac.jp) . JAPANESE JOURNAL OF CLINICAL ONCOLOGY, (1999 Feb) 29 (2) 74-7. Journal code: 0313225. ISSN: 0368-2811. Pub. country: Japan. Language: English.

AB BACKGROUND: The long-term survival of 200 patients with gastric cancer who underwent radical gastrectomy was analyzed with respect to the number and anatomical extent of lymph node metastasis. All of the patients received intra-**lymph node injection** of fine activated carbon particle solution (CH40) during surgery. METHODS: The average number of resected lymph nodes increased in line with the anatomical level of lymph node dissection; 32.5 per patient in D1, 42.3 in D2, 3 and 66.3 in D4. The percentage of blackened lymph nodes without metastasis (42.4%) was slightly higher than that of lymph nodes containing metastasis (37.2%), but the difference was not statistically significant. Of the 200 patients, 61 (30.5%) had microscopic evidence of metastatic lymph node involvement. Twenty-two patients had between one and three metastatic lymph nodes, 19 had between four and nine and 20 patients had more than nine. The 5-year survival rate was 93.1% in patients without lymph node metastasis, 71.9% in patients with 1-8 metastatic nodes, 36.1% in patients with 4-9 nodes and 19.2% in patients with > 9 nodes. RESULTS: The 5-year survival rate according to the anatomical extent of metastatic lymph nodes was 93.1% in n0, 63.1% in n1, 37.9% in n2, 27.8% in n3 and 0% in n4. The number of metastatic lymph nodes and also their anatomical extent were identified as independent prognostic factors for survival by multivariate analysis. CONCLUSION: The number and anatomical extent of metastatic lymph nodes have similar impacts on prognosis in gastric cancer.

L11 ANSWER 7 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 5

1998119836 EMBASE Revealing the in vivo behavior of CD4+ T Cells specific for an antigen expressed in Escherichia coli. Chen Z.-M.; Jenkins M.K.. Dr. M.K. Jenkins, Department of Microbiology, Center for Immunology, Univ. of Minnesota Medical School, 420 Delaware St. S.E., Minneapolis, MN 55455, United States. Journal of Immunology 160/7 (3462-3470) 1 Apr 1998. Refs: 29.
ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.

AB The clonal expansion and anatomic location of microbe-specific CD4+ The cells studied by tracking the fate of adoptively transferred DO11.10 TGR transgenic T cells specific for OVA peptide 323-339/I-A(d) in BALB/c mice infected s.c. with Escherichia coli expressing a MaIE-OVA fusion protein. After infection, the DO11.10 T cells accumulated in the T cell-rich paracortical regions of the draining lymph nodes, proliferated there for several days, and then moved into the B cell-rich follicies before they slowly disappeared from the lymph nodes. These changes occurred despite the fact that viable organisms were never found in the lymph nodes. The DO11.10 T cells also accumulated in the s.c. infection site, but about 1 day later than in the draining **lymph nodes**.
Injection of purified MaIE-OVA fusion protein alone induced a transient accumulation of D011.10 T cells in the paracortical regions, but these T cells never entered follicies and the mice did not produce anti-OVA antibodies. The DO11.10 T cells that survived in animals injected with MaIE-OVA alone were hyporesponsive to in vitro Ag restimulation and did not produce IL-2 and IFN-.gamma., whereas DO11.10 T cells from mice infected with MaIE-OVA-expressing bacteria produced both lymphokines. These results suggest that Ag-specific T cells are first activated in secondary lymphoid organs following primary bacterial infection and then migrate to the infection site. Furthermore, productive activation of the T

cells during the primary response is dependent on bacterial components other than the Ag itself.

L11 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
1998:506377 Document No. 129:312527 Purification and activity of mitochondrial aspartate aminotransferase from human liver. Li, Shaobing; Wei, Suzheng; Fang, Ding (Department of Gerontology, Hebei Medical University, Shijiazhuang, 050017, Peop. Rep. China). Hebei Yike Daxue Xuebao, 19(3), 149-152 (Chinese) 1998. CODEN: HEDXFQ. ISSN: 1007-3205. Publisher: Hebei Yike Daxue.
AB A method for extn. and purifn. of human liver mitochondrial aspartate aminotransferase (mAST) was established and used to prep. the rabbit antiserum for immunoassay. The mAST was extd. from human liver homogenate and isolated in satd. (NH4)2SO4 soln. after 55.degree.C water bath, and then purified by DEAE cellulose column and affinity chromatog. The specific activity of the purified mAST was 300000 U/mg protein, with SDS-PAGE identified to be homogeneous. Rabbit immunized with this purified mAST through **lymph node injection** gave the antiserum titer of 1:16.

L11 ANSWER 9 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 6
94242715 EMBASE Document No.: 1994242715. Migration of murine epidermal Langerhans cells to regional lymph nodes: Engagement of major histocompatibility complex class II antigens induces migration of Langerhans cells. Yamashita K.; Yano A.. Department of Medical Zoology, Nagasaki University, School of Medicine, 1-12-4 Sakamoto,Nagasaki 852, Japan. Microbiology and Immunology 38/7 (567-574) 1994.
ISSN: 0385-5600. CODEN: MIIMDV. Pub. Country: Japan. Language: English. Summary Language: English.
AB Langerhans cells are resident dendritic cells in the epidermis. Once they are loaded with epicutaneously-delivered antigens, they leave the epidermis and migrate to the regional lymph nodes where they initiate primary T cell responses as antigen-presenting cells. However, the stimulus that initiates such migration remains unknown. Because major histocompatibility complex class II (Ia) antigens on B lymphocytes or monocytic cells have been shown to function as signal transducers, we evaluated the effect of the engagement of Ia antigens on the migration of murine epidermal Langerhans cells. The intradermal injection of an anti-Ia monoclonaI antibody (mAb) reduced the density of Langerhans cells in epidermis and produced a dose- and time-dependent increase in the frequency of cells reactive with NLDC145 (Langerhans cell- and dendritic cell-specific mBb) within the regional **lymph nodes**. **Injection** of a control mAb had no effect. The NLDC145+ cells that were induced to accumulate in the regional lymph nodes were Ia+, large dendritic cells, some of which were positive for both NLDC145 and F4/80, a phenotype corresponding to that of murine epidermal Langerhans cells. Thus, the engagement of Ia antigens on Langerhans cells by mAb induces the migration of Langerhans cells from the epidermis to the regional lymph nodes. Analysis of these changes in Langerhans cells in vitro may help to reveal the biochemical sequence of events involved in the activation and differentiation of Langerhans cells.

L11 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
1994:153120 Document No. 120:153120 Intra-lymph nodal injection of a mixture of OK432 and mitomycin C cures distant lymph node metastasis. Okano, Shinji (1st Dep. Surg., Kyoto Prefect. Univ. Med., Kyoto, 602, Japan). Kyoto-furitsu Ika Daigaku Zasshi, 102(11), 1249-60 (English) 1993. CODEN: KFIZAO. ISSN: 0023-6012.
AB An immunochemotherapy consisting of the intra-lymph nodal injection of OK432 and mitomycin C was designed to treat lymph node metastasis in a syngeneic tumor-host system. P388 mouse leukemia cells (5 .times. 105 in 0.05 mL of normal saline) were inoculated s.c. into the left hind foot pad of BDF1 mice. Eight days after inoculation, the left popliteal and left lumbar lymph nodes became swollen with metastasis. The mice were

randomized into four groups 8 days after inoculation. Each mouse in the first group received an intra-lymph nodal injection of a mixt. of 0.5 KE OK432 and 25 .mu.g mitomycin C (MMC) in 0.1 mL of normal saline (MMC + OK I.L. group) into the left popliteal lymph node. The second group received an intra-lymph nodal injection of OK 432 (0.5 KE) in 0.1 mL of normal saline (OK I.L. group) into the same node. The third group received an intra-lymph nodal injection of MMC (25 .mu.g) in 0.1 mL of normal saline into the node and s.c. injection of OK432 (0.5 KE) in 0.1 mL of normal saline into the back (MMC I.L. + OK S.C. group). The last group received no drugs (control group). Three h after drug administration, each mouse underwent excision of the left popliteal lymph node and the left hind foot at the knee joint. Six days after excision, the left lumbar lymph node was transplanted i.p. to a recipient BDF1 mouse. The survival rate of the recipients was significantly higher in the MMC + OK I.L. group than in the other three groups. Microscopic views with hematoxylin-eosin staining showed lymphocyte infiltration into the left lumbar lymph node in the MMC + OK I.L. group. Winn's assay revealed that the infiltrating lymphocytes had killer activities against P388 cells. In conclusion, the intra-lymph nodal injection of mitomycin C and OK 432 is an effective immunochemotherapeutic mode for treatment of lymph node metastasis.

L11 ANSWER 11 OF 24 MEDLINE on STN DUPLICATE 7

87034973 Document Number: 87034973. PubMed ID: 3772106. Lymph node primary immunization of mice for the production of polyclonal and monoclonal antibodies. Raymond Y; Suh M. JOURNAL OF IMMUNOLOGICAL METHODS, (1986 Oct 23) 93 (1) 103-6. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Primary immunization of mice by **lymph node injection** of bovine serum albumin (BSA) in doses as low as 1 ng followed by a secondary immunization with 1 microgram each for intraperiteonal and intravenous injections was sufficient to elicit the production of circulating antibodies. The lowest efficient dose tested was the injection of 100 ng of BSA in the lymph nodes and booster injections of 1 ng each. This method was extended to the production of monoclonal antibodies using less than 20 micrograms of a 35 kDa polypeptide purified from hamster cells transformed by Herpes simplex type 2 viruses.

L11 ANSWER 12 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 8

84134295 EMBASE Document No.: 1984134295. Kinetics of cytotoxic lymphocytes in efferent lymph from single lymph nodes following immunization with vaccinia virus. Issekutz T.B.. Department of Pediatrics, Dalhousie University, Halifax, NS, Canada. Clinical and Experimental Immunology 56/3 (515-523) 1984.
CODEN: CEXIAL. Pub. Country: United Kingdom. Language: English.

AB Efferent lymphocytes collected from a cannulated lymphatic draining single lymph nodes were studied for their cytotoxic activity following the injection of live vaccinia virus subcutaneously into the drainage site of a **lymph node**. **Injection** of virus produced a 40-fold increase in the lymphoblast output 7 days following virus injection. Cytotoxic lymphocytes were detectable in lymph shortly after the appearance of lymphoblasts at 80 h and also reached a maximum during the 7th day. This was followed by a rapid decline of the cytotoxic cells although cytotoxic cells were detectable up to 2 weeks. The cytotoxic activity in lymph was found to be antigen specific, dependent on the effector/target cell ratio, and allogeneically restricted, indicating that it was most likely due to cytotoxic T lymphocytes (CTL). CTL precursors were found in large numbers in efferent lymph and appeared at approximately the same time as the mature CTL. Unlike CTL, the precursors became part of the recirculating lymphocyte pool and were detectable in efferent lymph for at least 2 months. Following a secondary challenge with vaccinia, lymphoblasts and CTL appeared at least 36 h earlier in the lymph. In summary, we have demonstrated that virus specific CTL are found in the efferent lymph collected from a single immunized lymph node in

sheep. The kinetics of the CTL and CTL precursors indicate that these lymphocytes are one of the earliest antigen specific cells detectable in efferent lymph and suggests that these cells migrate rapidly from the lymph node into efferent lymph for dissemination throughout the host to sites of virus infection.

L11 ANSWER 13 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
78305235 EMBASE Document No.: 1978305235. [Investigation of the lymphatic system using radioactive isotopes. Lymphogammagraphy]. EXPLORACION DEL SISTEMA LINFATICO CON ISOTOPOS RADIACTIVOS. LINFOGAMMAGRAFIA. Gil Gayarre M.; Delgado Macias T.; Meiggs Corbella L.; et al.. Cat. Radiol. Med. Fis., Fac. Med., Univ. Complutense, Madrid, Spain. Rehabilitacion 12/1 (53-60) 1978.
CODEN: RHTNAW. Pub. Country: Spain. Language: Spanish.
AB This technique makes it possible to visualize the parasternal, infraclavicular and subdiaphragmatic lymph nodes. The internal mammary chain is difficult to visualize. It is achieved by subcutaneous injection through the nipple. For study of the axillary **lymph nodes injection** is into the interdigital space of the hand.

L11 ANSWER 14 OF 24 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
1979:221604 Document No.: BA68:24108. THE EFFECT OF P CHLOROPHENYL ALANINE ON THE LYMPHATIC SYSTEM LYMPH NODES. FICEK W; TANGAPREGASSOM A M; TANGAPREGASSOM M J; LANTIN N. ANIM. PHYSIOL. DEP., JAGIELLONIAN UNIV., KRUPNICZA 50, 30-060 CRACOW, POL.. BULL ACAD POL SCI SER SCI BIOL, (1977 (RECD 1978)) 25 (12), 799-802. CODEN: BAPBAN. ISSN: 0001-4087. Language: English.
AB The experiment was carried out on male Wistar rats. After an i.p. injection of 200 mg of pCPA/kg body wt, stimulation of lymph papulae was noted. Lymphocytes forming there grouped themselves around the papulae on the site of the **lymph nodes**. **Injection** of 500 mg of pCPA/kg body wt caused grouping of numerous lymphocytes in the lymph nodes in the form of Blended mass around which numerous macrophages were seen.

L11 ANSWER 15 OF 24 MEDLINE on STN DUPLICATE 9
76212313 Document Number: 76212313. PubMed ID: 819381. Reevaluation of inguinal **lymph node injection** for production of adjuvant arthritis in the rat. Koga T; Sande B V; Yeaton R; Pearson C M. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1976) 51 (3) 359-67. Journal code: 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.
AB An experiment was designed to compare the efficiency of **lymph node injection** for the induction of adjuvant arthritis (AA) with that of conventional footpad injection in the rat. Quantitative studies revealed that the minimal dose required for induction of AA by the lymph node route is one fifth of that by the footpad route. Thus, the lymph node route was found to be more efficient than the footpad method in terms of higher incidence and earlier onset of AA. PPD in Freund's incomplete adjuvant was able to produce tuberculin sensitization in the rat. The lymph node route again proved to be superior in terms of consistent appearance of the 24-hour reaction on days 8 and 14 and prolongation of the skin reaction over 48 h. These findings show that the lymph node method is so efficient in the rat that it will be especially useful for the trial induction of AA with various materials of unknown potency as well as for production of delayed hypersensitivity. In addition, this injection method appears to be a simple and efficient technique for assay of other immunological reactions.

L11 ANSWER 16 OF 24 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
76:270262 The Genuine Article (R) Number: BZ435. RE-EVALUATION OF INGUINAL **LYMPH-NODE INJECTION** FOR PRODUCTION OF ADJUVANT ARTHRITIS IN RAT. KOGA T (Reprint); VANDESANDE B; YEATON R;

PEARSON C M. KYUSHU UNIV, SCH DENT, DEPT BIOCHEM, FUKUOKA 812, JAPAN; UNIV CALIF LOS ANGELES, DEPT MED, DIV RHEUMATOL, LOS ANGELES, CA, 90024. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY (1976) Vol. 51, No. 3, pp. 359-367. Pub. country: JAPAN; USA. Language: ENGLISH.

L11 ANSWER 17 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 10

75168694 EMBASE Document No.: 1975168694. Blood brain barrier and DNA changes during the evolution of experimental allergic encephalomyelitis. Oldendorf W.H.; Towner H.F.. Res. Serv., Wadsworth Hosp. Cent., VA, Los Angeles, Calif. 90073, United States. Journal of Neuropathology and Experimental Neurology 33/5 (616-631) 1974.
CODEN: JNENAD. Language: English.

AB Spinal cord and brain distribution spaces of 3H mannitol (MW 182) and 14C dextran (MW 60,000-90,000) were measured in rats during the development of EAE. These distribution spaces were used as indicators of the permeability of brain vasculature. This permeability was compared with appearance of neurological signs and cellular infiltration. Small cell infiltration was compared with increase of tissue DNA concentration. Neurological deficit appeared on about the 8th day after induction and remained confined to spinal cord, never involving cerebrum. Neurological deficit, small cell infiltration, a rise in mannitol and dextran distribution spaces and DNA elevation all first appeared at approximately the same time. Neurological deficit appeared in the caudal end of the cord and proceeded rostrally. Cellular infiltration, tracer distribution spaces and DNA increases followed the same pattern. Neither the ascending disease pattern nor other aspects of the disease were altered by the use of cerebral vs. spinal cord antigen or cervical vs. inguinal **lymph node injection**. The absolute increase in distribution spaces of mannitol was greater than dextran, indicating a correlation of increased vascular permeability with molecular size of the test tracer.

L11 ANSWER 18 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

74050893 EMBASE Document No.: 1974050893. Polyarthritis induced in the rat with cell walls from several bacteria and two Streptomyces species. Koga T.; Pearson C.M.; Narita T.; Kotani S.. Div. Rheumatol., Dept. Med., UCLA Sch. Med., Los Angeles, Calif. 90024, United States. Proceedings of the Society for Experimental Biology and Medicine 143/3 (824-827) 1973.
CODEN: PSEBAA. Language: English.

AB Various cell wall preparations from 9 different gram positive strains were tested for polyarthritis induction in the Lewis rat by the **lymph node injection** method. A striking arthritogenic capability of the cell walls of M. bovis, BCG, and C. diphtheria was noted to be essentially equivalent to that of M. tuberculosis. The cell walls from Streptomyces fradiae and lavendulae, L. plantarum, and S. aureus were less potent, and several other bacterial strains were not arthritogenic at all. However, when high molecular weight water soluble fractions were isolated from some of these strains, they too were often found to be arthritogenic, when administered in water in oil emulsions.

L11 ANSWER 19 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

74039126 EMBASE Document No.: 1974039126. Cyclic kinetics and mathematical expression of the primary immune response of soluble antigen. III. Cellular activity of antigen. Levi M.I.; Durikhin K.V.; Basova N.N.. Cent. Contr. Res. Lab., Munic. Disinfect. Stat., Moscow, Russia. Folia Microbiologica 18/4 (308-314) 1973.
CODEN: FOMIAZ. Language: English.

AB The cellular activity of an antigen is understood as its power to cause plasma cells to accumulate in the regional lymph node. Two plasma cell units (PCU) is the dose causing one plasma cell addition (as compared with the 'background'), whereas 1 PCU causes neither increase nor decrease in plasma cell number in the regional **lymph node**. **Injection** of antigen in less than 1 PCU causes plasma cells to

decrease in number. Interrelation between antigen and plasma cells changes with time in different regions of the lymphatic system.

L11 ANSWER 20 OF 24 MEDLINE on STN DUPLICATE 11
71156595 Document Number: 71156595. PubMed ID: 5551352. The effect of anti-lymphocytic antibody on the development of experimental thyroiditis in rats induced by the intra-**lymph node injection** of rat thyroglobulin in Freund's complete adjuvant. Kalden J R; James K. IMMUNOLOGY, (1971 Mar) 20 (3) 269-75. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

L11 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
1970:75087 Document No. 72:75087 Development of a radioimmunoassay for oxytocin: radioiodination, antibody production, and separation techniques. Chard, T.; Kitau, M. J.; Landon, J. (Dep. Chem. Pathol., St. Bartholomew's Hosp. Med. Sch., London, UK). Journal of Endocrinology, 46(2), 269-78 (English) 1970. CODEN: JOENAK. ISSN: 0022-0795.
AB A simple and rapid method is described for labeling oxytocin with 131I at a high specific activity. This method is compared with those of previous workers. A satisfactory antiserum has been raised by direct intra-**lymph node injection** of oxytocin adsorbed to C microparticles. Methods for sepg. antibody-bound from free oxytocin are described, and reasons given for preferring a procedure using (NH4)2SO4 pptn. These data form the basis for developing a radioimmunoassay intended for the detn. of oxytocin in human plasma.

L11 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
1969:458997 Document No. 71:58997 Antigenic heterogeneity of chicken 7S immunoglobulin. Wilkinson, P. C.; French, Valentine I. (Univ. Glasgow, Glasgow, UK). Immunochemistry, 6(3), 498-501 (English) 1969. CODEN: IMCHAZ. ISSN: 0019-2791.
AB Serums from chickens immunized with human serum albumin, examd. by radioimmunoelectrophoresis for the presence of antigen-binding globulins, contained such proteins in the 7S and 19S arcs. Egg yolk contained only 7S HSA immunoglobulin, in an arc with 2 cathodal tails which met in a reaction of partial identity at their anodal ends. Both cathodal tails reacted with heavy-chain antiserum. Monospecific antiserums were raised in rabbits by intra-**lymph node injection** of the agar gel containing the antigen-antibody complexes.

L11 ANSWER 23 OF 24 MEDLINE on STN DUPLICATE 12
68049414 Document Number: 68049414. PubMed ID: 4293839. Lymphangiography by **lymph-node injection**. Hall R C; Krementz E T. JAMA, (1967 Dec 25) 202 (13) 1136-9. Journal code: 7501160. ISSN: 0098-7484. Pub. country: United States. Language: English.

L11 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
1935:1547 Document No. 29:1547 Original Reference No. 29:223g-h The cellular response of lymph nodes to various dust suspensions introduced into lymphatics. Stuber, Katharina Journal of Industrial Hygiene, 16, 282-95 (Unavailable) 1934. CODEN: JIDHAN. ISSN: 0095-9022.
AB Distd. water suspensions of silica, granite, rhodenite, talc, asbestos, limestone, CdS, MnO2, rouge and cornstarch were injected into the lymphatic that accompanies the external saphenous and cephalic veins, resp. The **lymph-node injection** method may be developed into a rapid means of detg. the toxicity of certain dusts. The silica-contg. cells lost their phagocytic power toward other particulate matter to a considerable degree and are identified biologically as modified endothelial lymph phagocytes.

=> s lymph node injection
L12 45 LYMPH NODE INJECTION

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=> s l12 and CTL response
L13           0 L12 AND CTL RESPONSE

=> s CTL response
L14       14238 CTL RESPONSE

=> s l14 and memory
L15        1246 L14 AND MEMORY

=> s l15 and lymphatic injection
L16           0 L15 AND LYMPHATIC INJECTION

=> s l15 and cancer
L17          71 L15 AND CANCER

=> s l17 and tumor
L18          49 L17 AND TUMOR

=> s l18 and CTL
L19          49 L18 AND CTL

=> s l19 and injection
L20           9 L19 AND INJECTION

=> dup remove l20
PROCESSING COMPLETED FOR L20
L21           6 DUP REMOVE L20 (3 DUPLICATES REMOVED)

=> d l21 1-6 cbib abs

L21  ANSWER 1 OF 6  EMBASE  COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
2003286716  EMBASE  Immunological evaluation of CTL
     precursor-oriented vaccines for advanced lung cancer patients.
     Mine T.; Gouhara R.; Hida N.; Imai N.; Azuma K.; Rikimaru T.; Katagiri K.;
     Nishikori M.; Sukehiro A.; Nakagawa M.; Yamada A.; Aizawa H.; Shirouzu K.;
     Itoh K.; Yamana H.. T. Mine, Department of Immunology, Kurume University
     School of Medicine, 67 Asahi-machi, Kurume 830-0011, Japan.
     mine@med.kurume-u.ac.jp. Cancer Science  94/6 (548-556)  1 Jun 2003.
     Refs: 31.
     ISSN: 1347-9032. CODEN: CSACCM. Pub. Country: Japan. Language: English.
     Summary Language: English.
AB   Recent clinical trials of peptide vaccine for cancer patients
     have rarely resulted in tumor regression. One of the reasons for
     this failure could be an insufficient induction of anti-tumor
     responses in these regimens, in which peptide-specific memory
     cytotoxic T lymphocytes (CTLs) were not measured prior to
     vaccination. We investigated in this study whether pre-vaccination
     measurement of peptide-specific CTLs can provide any advantages
     in lung cancer patients receiving peptide vaccination with
     regard to safety and immunological responses. Ten patients with advanced
     lung cancer received vaccination with peptides under a regimen
     of CTL precursor-oriented vaccination, in which pre-vaccination
     peripheral blood mononuclear cells (PBMCs) were at first screened for
     reactivity in vitro to each of 14 peptides, followed by in vivo
     administration of only the reactive peptides. Profiles of the vaccinated
     peptides varied markedly among the 10 patients. This regimen was generally
     well-tolerated, although local skin reactions, diarrhea, and colitis were
     observed in 8, 2, and 1 patient, respectively. Increased CTL
     responses against the immunized peptides and tumor cells
     were observed in the post-vaccination PBMCs from 4 of 8 and 3 of 10
     patients tested, respectively. Peptide-specific lgG became detectable in
     post-vaccination sera in 4 of 10 patients tested, and these 4 patients had
     a long progression-free survival. Furthermore, the median survival time of
     9 patients with non-small cell lung cancer was 668.0.+-.164.2
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days. These results encourage further development of **CTL** precursor-oriented peptide vaccination for lung **cancer** patients.

L21 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
2002690599 Document Number: 22316663. PubMed ID: 12429628. Toxicity, immunogenicity, and induction of E75-specific **tumor**-lytic **CTLs** by HER-2 peptide E75 (369-377) combined with granulocyte macrophage colony-stimulating factor in HLA-A2+ patients with metastatic breast and ovarian **cancer**. Murray James L; Gillogly Michael E; Przepiorka Donna; Brewer Hannah; Ibrahim Nuhad K; Booser Daniel J; Hortobagyi Gabriel N; Kudelka Andrzej P; Grabstein Kenneth H; Cheever Martin A; Ioannides Constantin G. (Department of Bioimmunotherapy, M. D. Anderson Cancer Center, Houston, Texas 77030, USA.) CLINICAL CANCER RESEARCH, (2002 Nov) 8 (11) 3407-18. Journal code: 9502500. ISSN: 1078-0432. Pub. country: United States. Language: English.

AB To determine the toxicity and immunogenicity of the HER-2/neu, HLA-A2-restricted peptide E75 in patients with metastatic breast and ovarian **cancer**, 14 patients were vaccinated with escalating amounts of E75 (100, 500, and 1000 microg) mixed with 250 microg granulocyte macrophage colony-stimulating factor as adjuvant. Each vaccine dose was administered in a total volume of 1.5 ml divided into four intradermal **injections** and administered weekly for 4 weeks, followed by monthly boosts for a total of 10 **injections**. Vaccinations were well tolerated without significant toxicity. Blood was drawn before, at 8 weeks, and up to 13-16 months after vaccination for measurement of cellular immunity. Seven of 8 patients tested had significant delayed type hypersensitivity to E75 defined as >5 mm induration. Peripheral blood mononuclear cells from 5 of 9 patients tested proliferated to E75 with a stimulation index of > or = 2.0. Of 8 vaccinated patients tested for induction of a **CTL response**, 4 responded to stimulation by autologous dendritic cells plus cytokines by eliciting E75-specific lytic activity consistent with the presence of activated/**memory** cells, 2 others after in vitro stimulation with E75 + interleukin-12 +/- anti-CD152(33KD), whereas 2 others did not respond. Four patients with E75-specific **CTLs** present specifically recognized E75 on indicator **tumors** as demonstrated by cold-target inhibition of **tumor** lysis. These 4 patients showed E75-specific IFN-gamma production. peripheral blood mononuclear cell from 3 of these patients proliferated to E75, but stimulation indices were higher in the prevaccine samples. All 4 of the patients showed DTH responses to E75. These results demonstrate that vaccination with E75+ granulocyte macrophage colony-stimulating factor can induce both peptide-specific IFN-gamma and epitope specific **CTLs** , which lyse HER-2/neu+ **tumors** in stage IV patients.

L21 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
2001:283811 Document No. 134:294515 Archaeosomes as immunomodulating carriers for acellular vaccines to induce cytotoxic T lymphocyte (**CTL**) **responses** and protect the vaccinated host against intracellular pathogens and **cancer**. Sprott, G. Dennis; Krishnan, Lakshmi; Conlan, J. Wayne; Omri, Abdel; Patel, Girishchandra B. (National Research Council of Canada, Can.). PCT Int. Appl. WO 2001026683 A2 20010419, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-CA1197 20001012. PRIORITY: US 1999-PV158944 19991012; US 2000-PV209988 20000608.

AB The invention provides methods and compns. useful for inducing major histocompatibility complex class-I (MHC-I)-restricted cytotoxic T lymphocyte (**CTL**) **response** in a mammalian host

immunized with acellular (non-replicating) antigen. The methods comprise using a liposome, an archaeosome, comprising a polar lipid ext. of an archaeobacterium as both immune modulator and carrier for the non-replicating antigen. In addn. to a strong antigen-specific **CTL response**, the archaeosome adjuvant elicits CD4+ Th1, CD4+ Th2 (antibody), and **memory** responses to the acellular antigen in the vaccine compn. The invention provides methods for mounting a rapid, and a long lasting protective immunity in the vaccinated host against infections caused by intracellular pathogens, esp. those that require the host to mount an antigen-specific CD8+ T cell immune response for the protection. The methods of the invention are also useful in, but not restricted to, vaccines for preventing or reducing growth of solid **tumors**.

L21 ANSWER 4 OF 6 MEDLINE on STN
2001259446 Document Number: 21136365. PubMed ID: 11238635. CTLA-4 blockade enhances the **CTL responses** to the p53 self-**tumor** antigen. Hernandez J; Ko A; Sherman L A. (Department of Immunology, The Scripps Research Institute, La Jolla, CA 92037, USA.) JOURNAL OF IMMUNOLOGY, (2001 Mar 15) 166 (6) 3908-14. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB p53 is an attractive target for **cancer** immunotherapy because it is overexpressed in a high proportion of many different types of **tumors**. However, it is also expressed in normal tissues and acts as a toleragen in vivo. Previously, detailed examination of the repertoire specific for the murine p53(261-269) epitope in conventional and p53-deficient mice demonstrated that because of expression of p53, the CD8(+) T cells that respond to this epitope express low-affinity TCRs. It has been reported that tolerance to **tumor** Ags can be broken by in vivo administration of anti-CTLA-4 mAb. With the goal of overriding tolerance and achieving optimal activation of p53-specific **CTL**, the current study has assessed the effect of anti-CTLA-4 mAb on the p53-specific repertoire. It was found that blockade of CTLA-4 engagement at the time of antigenic stimulation induced a vigorous amplification of the **CTL responses** to p53 as well as proportionate expansion of the **memory** T cell pool. This effect was dependent on the presence of CD4(+) T cell help and correlated with an enhancement of helper function. However, anti-CTLA-4 treatment did not enhance the avidity of the resultant p53-specific **CTL** populations and, therefore, could not reverse this important consequence of tolerance.

L21 ANSWER 5 OF 6 MEDLINE on STN
1998129331 Document Number: 98129331. PubMed ID: 9469429. Delivery of multiple CD8 cytotoxic T cell epitopes by DNA vaccination. Thomson S A; Sherritt M A; Medveczky J; Elliott S L; Moss D J; Fernando G J; Brown L E; Suhrbier A. (The Cooperative Research Centre for Vaccine Technology, Queensland Institute of Medical Research, Brisbane, Australia.) JOURNAL OF IMMUNOLOGY, (1998 Feb 15) 160 (4) 1717-23. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB Development of CD8 alphabeta **CTL** epitope-based vaccines requires an effective strategy capable of co-delivering large numbers of **CTL** epitopes. Here we describe a DNA plasmid encoding a polyepitope or "polytope" protein, which contained multiple contiguous minimal murine **CTL** epitopes. Mice vaccinated with this plasmid made MHC-restricted **CTL responses** to each of the epitopes, and protective **CTL** were demonstrated in recombinant vaccinia virus, influenza virus, and **tumor** challenge models. **CTL responses** generated by polytope DNA plasmid vaccination lasted for 1 yr, could be enhanced by co-delivering a gene for granulocyte-macrophage CSF, and appeared to be induced in the absence of CD4 T cell-mediated help. The ability to deliver large numbers of **CTL** epitopes using relatively small polytope constructs and DNA vaccination technology should find application in the design of human epitope-based **CTL** vaccines, in particular in vaccines against EBV, HIV, and certain **cancers**.

L21 ANSWER 6 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

76050807 EMBASE Document No.: 1976050807. Primary and secondary in vitro generation of cytolytic T lymphocytes in the murine sarcoma virus system. Plata F.; Cerottini J.C.; Brunner K.T.. Ludwig Inst. Cancer Res., Lausanne, Switzerland. European Journal of Immunology 5/4 (227-233) 1975.
CODEN: EJIMAF. Language: English.

AB Cell mediated cytotoxic responses in vitro to surface antigens associated with murine sarcoma virus (MSV) induced **tumors** were investigated using mixed leukocyte **tumor** cell cultures (MLTC). The source of responding cells was either spleens from normal C57Bl/6 mice primary MLTC or spleens from C57Bl/6 mice carrying or having rejected a MSV induced **tumor** (secondary MLTC). Graffi virus induced Gil 4 leukemia cells, Rauscher virus induced RB1 5 leukemia cells, and MSV induced MSV B16 sarcoma cells were used as stimulating syngeneic **tumor** cells and/or target cells. Under appropriate culture conditions, cytolytic T lymphocytes (**CTL**) were generated in both primary and secondary MLTC. As assessed by a quantitative short term 51Cr release assay system, **CTL** activity in secondary MLTC populations was at least 10 fold higher than that in primary MLTC populations, and 100 fold higher than that in spleen cells taken at the peak of the in vivo response of MSV infected mice. The ability of spleen cells to mount a secondary **CTL response** in vitro could be observed as early as 5 days after virus **injection**, increased up to the time of maximum **tumor** size and persisted long after **tumor** regression. This suggests the development of increased numbers of **CTL** progenitors and/or the formation of '**memory**' **CTL** in spleens of MSV injected mice.

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=> s antigen delivery
L22        1734 ANTIGEN DELIVERY

=> s l22 and lymph node
L23          91 L22 AND LYMPH NODE

=> s l23 and CTL
L24          10 L23 AND CTL

=> dup remove l24
PROCESSING COMPLETED FOR L24
L25           6 DUP REMOVE L24 (4 DUPLICATES REMOVED)

=> d l25 1-6 cbib abs
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L25 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1

2002189889 Document Number: 21920352. PubMed ID: 11922620. Investigation of **antigen delivery** route in vivo and imune-boosting effects mediated by pH-sensitive liposomes encapsulated with K(b)-restricted **CTL** epitope. Lee Ki-Young; Chun Eunyoung; Seong Baik L. (Department of Biotechnology, College of Engineering and Bioproducts Research Center, Yonsei University, 134 Shinchon-Dong, Seodaemun-Gu, Seoul, 120-749, South Korea.) BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2002 Apr 5) 292 (3) 682-8. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Using fluorescein isothiocyanate (FITC)-conjugated H-2K(b) **CTL** epitope (SIINFEKL) as a model system, we investigated the **antigen delivery** route by pH-sensitive liposomes in vivo. Fluorescence was initially detected in **lymph nodes** at 3 h after immunization, and its intensity reached a peak value in superticial inguinal **lymph node** at 9 h. No trace could be detected in spleen even with prolonged monitoring for up to 24 h. These results strongly suggest that the presentation of **CTL**-peptide

antigen vehicled by pH-sensitive liposomes exclusively occurs in **lymph nodes**. In mice immunized with the H-2K(b) **CTL** epitope encapsulated pH-sensitive liposomes, peptide-specific **CTL** response was detected at day 3. The response was strongly augmented by the second immunization and persisted up to at least 45 days. These results suggest that pH-sensitive liposome formula functions as a potential adjuvant of peptide antigens and is useful for the induction of antigen specific CTLsv in vivo.

L25 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
2001:656689 Document No. 135:317132 Recombinant Semliki Forest virus vaccine vectors: the route of injection determines the localization of vector RNA and subsequent T cell response. Colmenero, P.; Berglund, P.; Kambayashi, T.; Biberfeld, P.; Liljestrom, P.; Jondal, M. (Microbiology and Tumorbiology Center, Karolinska Institutet, Stockholm, S-171 77, Swed.). Gene Therapy, 8(17), 1307-1314 (English) 2001. CODEN: GETHEC. ISSN: 0969-7128. Publisher: Nature Publishing Group.

AB Vectors based on Semliki Forest virus (SFV) have been widely used in vitro and in vivo to express heterologous genes in animal cells. In particular, the ability of recombinant SFV (rSFV) to elicit specific, protective immune responses in animal models suggests that rSFV may be used as a vaccine vehicle. In this study, the authors examd. the distribution of rSFV in vivo by immunohistochem. and RT-PCR after i.v., i.m. and s.c. injection of rSFV particles and related this to the degree of cytotoxic T lymphocyte (**CTL**) responses and frequency of specific T cells detected by MHC-I tetramers. The authors found that after i.v. injection, rSFV-RNA was distributed to a variety of different tissues, whereas it was confined locally after i.m. and s.c. injections. The persistence of the rSFV vector was transient, and no viral RNA could be detected 10 days after inoculation. All tested routes of immunization generated significant levels of antigen-specific **CTL** responses and increased nos. of specific CD8+ T cells, as detected by tetramer binding. The distribution of antigen-specific **CTLs** correlated with the in vivo distribution pattern of rSFV, with a highest frequency in the spleen or local **lymph node**, depending on the injection route.

L25 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
2001:723569 Papers to Appear in Forthcoming Issues. Anon. Cellular Immunology, 211(1), 80 (English) 2001. CODEN: CLIMB8. ISSN: 0008-8749. Publisher: Academic Press.

AB (Received and Accepted Dates Follow Title)Roles of Intracellular Calcium and NF-kB in the Bacillus Calmette Guerin-Induced Secretion of Interleukin-8 from Human Monocytes. Patricia Mendez-Samperio, Janet Palma, and Abraham Vazquez. (Received 12/27/00; accepted 5/29/01.)Requirement for Sustained MAPK Signaling in Both CD4 and CD8 Lineage Commitment: A Threshold Model. Beverley Wilkenson and Jonathan Kaye. (Received 3/29/01; accepted 6/25/01.)Differential Effect of IL-4 and IL-13 on CD44 Expression in the Burkitt's Lymphoma B Cell Line BL30/B95-8 and in Epstein-Barr Virus (EBV) Transformed Human B Cells: Loss of IL-13 Receptors on Burkitt's Lymphoma B Cells. Katrina Gee, Maya Kozlowski, Marko Kryworuchko, Francisco Diaz-Mitoma, and Ashok Kumar. (Received 4/4/01; accepted 7/1/01.)Class Switch Recombination Signals Induce Lymphocyte-Derived Spo11 Expression and Spo11 Antisense Oligonucleotide Inhibits Class Switching. Haruhiko Tokuyama and Yukiko Tokuyama. (Received 2/28/01; accepted 7/2/01.)CD Antigens 2001. David Y. Mason, Pascale Andre, Armand Bensussan, Chris Buckley, C. Civin, E. Clark, M. de Haas, S. Goyert, M. Hadam, D. Hart, V. Horejsi, S. Meuer, J. Morrissey, R. Schwartz-Albiez, S. Shaw, D. Simmons, M. Uguccioni, E. van der Schoot, E. Vivier, and H. Zola. (Received 6/25/01; accepted 7/2/01.)Resistance to Malarial Infection is Achieved by the Cooperation of NK1.1+ and NK1.1- Subsets of Intermediate TCR Cells Which are Constituents of the Innate Immunity. M. Kaiissar Mannoor, Anura Weerasinghe, Ramesh C. Halder, Sufi Reza, M. Morshed, Anoja Ariyasinghe, Hisami Watanabe, Horoho Sekikawa, and Toru Abo. (Received 5/7/01; accepted 7/19/01.)IL-1B is Essential for Langerhans Cell Activation and **Antigen Delivery** to the

Lymph Nodes During Contact Sensitization: Evidence for a Dermal Source of IL-1B. Laurie P. Shornick, Alvin K. Bisarya, and David D. Chaplin. (Received 6/4/01; accepted 7/19/01.)Heterosubtypic Immunity Against Human Influenza A Viruses Including Recently Emerged Avian H5 and H9 Viruses Induced By Flu-ISCOM Vaccine in Mice Requires Both **CTL** and Macrophage Function. Suryaprakash Sambhara, Anjna Kurichh, Renata Miranda, Terrence Tumpey, Thomas Rowe, Mary Renshaw, Rita Arpino, Alan Tamane, Ali Kandil, Olive James, and Brian Underdown. (Received 4/17/01; accepted 7/24/01.). (c) 2001 Academic Press.

L25 ANSWER 4 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
2001:824559 The Genuine Article (R) Number: 480ZM. Induction and direction of immune responses by vaccine adjuvants. Schijns V E J C (Reprint). Intervet Int BV, Dept Vaccine Technol & Immunol, POB 31, NL-5830 AA Boxmeer, Netherlands (Reprint); Intervet Int BV, Dept Vaccine Technol & Immunol, NL-5830 AA Boxmeer, Netherlands. CRITICAL REVIEWS IN IMMUNOLOGY (SEP 2001) Vol. 21, No. 1-3, pp. 75-85. Publisher: BEGELL HOUSE INC. 79 MADISON AVE, SUITE 1205, NEW YORK, NY 10016-7892 USA. ISSN: 1040-8401. Pub. country: Netherlands. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Successful vaccination against infectious or neoplastic disease programs the host's immune system, in a multistep process, to generate an efficient defense and memory response. Conditioning of immune responses to nonreplicating, poorly immunogenic antigens generally requires the help of an adjuvant. The present review attempts to classify vaccine adjuvants functionally, according to recently proposed, mutually exclusive concepts of immunity induction. These include the geographical concept of immune reactivity and the theory of depot effect. Both emphasize the importance of **antigen delivery** and localization to the **lymph node** in time after immunization. Other concepts stress the importance of key signals, such as "infectious nonself" or "danger," which influence the activation state of the antigen-presenting cell (APC) and, hence, its capacity to prime naive T cells. The nature of adjuvant-induced immune responses is discussed in relation to each concept.

L25 ANSWER 5 OF 6 MEDLINE on STN
2001010193 Document Number: 20429625. PubMed ID: 10973219. Targeted **antigen delivery** to antigen-presenting cells including dendritic cells by engineered Fas-mediated apoptosis. Chattergoon M A; Kim J J; Yang J S; Robinson T M; Lee D J; Dentchev T; Wilson D M; Ayyavoo V; Weiner D B. (Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.) NATURE BIOTECHNOLOGY, (2000 Sep) 18 (9) 974-9. Journal code: 9604648. ISSN: 1087-0156. Pub. country: United States. Language: English.
AB Immunity to tumors as well as to viral and bacterial pathogens is often mediated by cytotoxic T lymphocytes (**CTLs**). Thus, the ability to induce a strong cell-mediated immune response is an important requirement of novel immunotherapies. Antigen-presenting cells (APCs), including dendritic cells (DCs), are specialized in initiating T-cell immunity. Harnessing this innate ability of these cells to acquire and present antigens, we sought to improve antigen presentation by targeting antigens directly to DCs in vivo through apoptosis. We engineered Fas-mediated apoptotic death of antigen-bearing cells in vivo by co-expressing the immunogen and Fas in the same cell. We then observed that the death of antigen-bearing cells results in increased antigen acquisition by APCs including DCs. This in vivo strategy led to enhanced antigen-specific **CTLs**, and the elaboration of T helper-1 (Th1) type cytokines and chemokines. This adjuvant approach has important implications for viral and nonviral delivery strategies for vaccines or gene therapies.

L25 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
97:40067 The Genuine Article (R) Number: WA137. Novel adjuvants and vaccine delivery systems. Morein B (Reprint); VillacresEriksson M; Sjolander A;

Bengtsson K L. SWEDISH UNIV AGR SCI, BOX 585, S-75123 UPPSALA, SWEDEN (Reprint); NATL VET INST, DEPT VIROL, BIOMED CTR, S-75123 UPPSALA, SWEDEN. VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY (NOV 1996) Vol. 54, No. 1-4, pp. 373-384. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0165-2427. Pub. country: SWEDEN. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Conventionally the efficiency of an adjuvant is measured by the capacity to induce enhanced antibody serum titres and cell mediated immunity (CMI) to a given antigen. Nowadays the capacity of an adjuvant is also measured by the quality as well as the magnitude of the induced immune response, guided by the protective immune response required. Quality includes isotype and IgG subclass responses, T-helper cell responses characterized by the cytokine profile and cytotoxic T cells (**CTL**), In the early phase of immunization some adjuvants influence the antigen administration and uptake by a so-called depot effect exemplified by aluminium hydroxide gel and oil adjuvants, which possibly is not as desired as alledged. A modem depot is exerted by slow release formulations continuously releasing the antigen over a period of time or by pulses at intervals aiming at 'single injection' vaccine. Great efforts are made to formulate efficient delivery formulations targeting the antigens from the site of administration, to draining **lymph nodes** or distant lymphatic tissue or to mucosal surfaces by parenteral or mucosal administrations. Nowadays, non-replicating carriers besides replicating vaccines are formulated to induce mucosal immune responses encompassing secretory IgA and CMI. Efforts to evoke immune responses on mucosal membranes distant from the site of administration have resulted mostly in little success. For a long time it was considered that **CTL** under the restriction of MHC Class I only could be evoked by replicating viruses or intracellular parasites, However, novel adjuvant delivery systems readily induce **CTL** by delivering the antigen to the APC resulting in intracellular transport to the cytosol for the MHC Class I presentation system, as well as to the endosomal pathway for the MHC Class II presentation.

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=> s (kundig t?/au or simard j?/au)
L26        1832 (KUNDIG T?/AU OR SIMARD J?/AU)

=> s l26 and CTL response
L27          19 L26 AND CTL RESPONSE

=> dup remove l27
PROCESSING COMPLETED FOR L27
L28            6 DUP REMOVE L27 (13 DUPLICATES REMOVED)

=> d l28 1-6 cbib abs

L28  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2003 ACS on STN
2002:52003   Document No. 136:117371  Method of inducing an immunological
     CTL response by lymphatic system delivery of peptide
     vaccine.  Kundig, Thomas M.; Simard, John J. L.
     (Switz.).  U.S. Pat. Appl. Publ. US 2002007173 A1 20020117, 48 pp.,
     Cont.-in-part of U. S. Ser. No. 380,534.  (English).  CODEN: USXXCO.
     APPLICATION: US 2001-776232 20010202.  PRIORITY: CA 1997-2209815 19970710;
     US 1997-988320 19971210; WO 1998-US14289 19980710; US 1999-380534
     19990901.
AB   Disclosed herein are methods for inducing an immunol. CTL
     response to an antigen by sustained, regular delivery of the
     antigen to a mammal so that the antigen reaches the lymphatic system.
     Antigen is delivered at a level sufficient to induce an immunol.
     CTL response in a mammal and the level of the antigen in
     the mammal's lymphatic system is maintained over time sufficient to
     maintain the immunol. CTL response.  Also disclosed is
     an article of manuf. for delivering an antigen that induces a CTL
     response in an animal.  The antigen can be used in vaccines for
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cancer or infection.

L28 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
2002152378 Document Number: 21881762. PubMed ID: 11884458. Critical role for activation of antigen-presenting cells in priming of cytotoxic T cell responses after vaccination with virus-like particles. Storni Tazio; Lechner Franziska; Erdmann Iris; Bachi Thomas; Jegerlehner Andrea; Dumrese Tilman; **Kundig Thomas M**; Ruedl Christiane; Bachmann Martin F. (Cytos Biotechnology, AG, Department of Dermatology and Institute of Experimental Immunology, University Hospital, and Elektronenmikroskopisches Zentrallabor Universitat, Zurich, Switzerland.) JOURNAL OF IMMUNOLOGY, (2002 Mar 15) 168 (6) 2880-6. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB Virus-like particles (VLPs) are known to induce strong Ab responses in the absence of adjuvants. In addition, VLPs are able to prime **CTL responses** in vivo. To study the efficiency of this latter process, we fused peptide p33 derived from lymphocytic choriomeningitis virus to the hepatitis B core Ag, which spontaneously assembles into VLPs (p33-VLPs). These p33-VLPs were efficiently processed in vitro and in vivo for MHC class I presentation. Nevertheless, p33-VLPs induced weak **CTL responses** that failed to mediate effective protection from viral challenge. However, if APCs were activated concomitantly in vivo using either anti-CD40 Abs or CpG oligonucleotides, the **CTL responses** induced were fully protective against infection with lymphocytic choriomeningitis virus or recombinant vaccinia virus. Moreover, these **CTL responses** were comparable to responses generally induced by live vaccines, because they could be measured in primary ex vivo (51)Cr release assays. Thus, while VLPs alone are inefficient at inducing **CTL responses**, they become very powerful vaccines if applied together with substances that activate APCs.

L28 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
1999:64705 Document No. 130:138281 A method of inducing a **CTL response**. **Kundig, Thomas M.; Simard, John J. L.** (CTL Immunotherapies Corporation, Can.). PCT Int. Appl. WO 9902183 A2 19990121, 199 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US14289 19980710. PRIORITY: CA 1997-2209815 19970710; US 1997-988320 19971210.
AB A method of inducing a cytotoxic T-lymphocyte (**CTL**) **response** to an antigen is disclosed. The method involves delivering the antigen to the lymphatic system of an animal regularly over a sustained period of time using, e.g., an osmotic pump. The method is advantageous over prior art methods for inducing a **CTL response** in that it does not require repetitive immunizations or the use of adjuvants. The method of the present invention can be used for the induction of CTLs in tumor or infectious disease immunotherapy.

L28 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 2
96261644 Document Number: 96261644. PubMed ID: 8666900. LFA-1-deficient mice show normal **CTL responses** to virus but fail to reject immunogenic tumor. Schmits R; **Kundig T M**; Baker D M; Shumaker G; **Simard J J**; Duncan G; Wakeham A; Shahinian A; van der Heiden A; Bachmann M F; Ohashi P S; Mak T W; Hickstein D D. (Amgen Institute, Ontario Cancer Institute, Department of Medical Biophysics, Toronto, Canada.) JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Apr 1) 183 (4) 1415-26. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.
AB The leukocyte integrin LFA-1 (CD11a/CD18) plays an important role in

lymphocyte recirculation and homotypic interactions. Leukocytes from mice lacking CD11a displayed defects in in vitro homotypic aggregation, in proliferation in mixed lymphocyte reactions, and in response to mitogen. Mutant mice mounted normal cytotoxic T cell (**CTL**) **responses** against systemic LCMV and VSV infections and showed normal ex vivo CTL function. However, LFA-1-deficient mice did not reject immunogenic tumors grafted into footpads and did not demonstrate priming response against tumor-specific antigen. Thus CD11a deficiency causes a selective defect in induction of peripheral immune responses whereas responses to systemic infection are normal.

L28 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 3
93246658 Document Number: 93246658. PubMed ID: 8097755. Nonimmunogenic tumor cells may efficiently restimulate tumor antigen-specific cytotoxic T cells. **Kundig T M**; Bachmann M F; Lefrancois L; Puddington L; Hengartner H; Zinkernagel R M. (Institute of Experimental Immunology, University of Zurich, Switzerland.) JOURNAL OF IMMUNOLOGY, (1993 May 15) 150 (10) 4450-6. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Induction of immunity to a viral protein that had been transfected into a tumor cell line was studied. The nucleoprotein (NP) of vesicular stomatitis virus (VSV) was used as a model tumor-associated Ag after transfection into EL-4, and H-2b thymoma originating from C57BL/6 mice. The NP-transfected cell line (EL-4NP) was lysed by NP-specific CTL and was found to restimulate NP-specific CTL in vitro as efficiently as did VSV-infected macrophages. Despite both of these in vitro characteristics, C57BL/6 mice inoculated with EL-4NP did not mount a measurable NP-specific **CTL response** and developed a lethal tumor as rapidly as did mice given control EL-4. This lack of immunogenicity could not be explained by down-regulation of MHC class I molecules or by loss of NP; even EL-4NP cells metastasizing to the spleen kept their high restimulatory capacity and excellent target characteristics. However, once mice were immunized with VSV or with a vaccinia-VSV-NP recombinant virus they were protected against tumor growth of EL-4NP by CD8+ CTL but not by CD4+ T cells. Taken together, the failure of the tumor-associated Ag to induce a protective T cell response in vivo despite its excellent capacity to restimulate CTL in vitro may encourage adjuvant immunotherapy in cancer; even the effects of weakly immunizing tumor vaccines, e.g., recombinant viruses, may be efficiently amplified by tumor cells.

L28 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 4
94112120 Document Number: 94112120. PubMed ID: 7904347. CD4 negative mice as a model for immunodeficiency. Rahemtulla A; Shahinian A; **Kundig T**; Zinkernagel R; Mak T W. (Amgen Institute, Toronto, Ontario, Canada.) PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON. SERIES B: BIOLOGICAL SCIENCES, (1993 Oct 29) 342 (1299) 57-8. Journal code: 7503623. ISSN: 0962-8436. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD4 is a co-receptor required for T cell helper functions. A mouse strain without CD4 expression has been generated. These animals, surprisingly have a normal **CTL response** and reduced, but not absent, humoral responses. A new population of MHC class II restricted CD4-CD8-TcR alpha beta+ T cells has emerged which possess helper function potential. These findings have important implications on disease situations where CD4 cells are decreased or absent.

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=> s antigen delivery
L29       1734 ANTIGEN DELIVERY

=> s l29 and pump
L30         17 L29 AND PUMP

=> s l30 and lymph node
L31          0 L30 AND LYMPH NODE
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=> s l30 and lymphatic tissue
L32 0 L30 AND LYMPHATIC TISSUE

=> s spleen injection
L33 60 SPLEEN INJECTION

=> s l33 and CTL
L34 0 L33 AND CTL

=> s l33 and antigen
L35 20 L33 AND ANTIGEN

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PROCESSING COMPLETED FOR L35
L36 10 DUP REMOVE L35 (10 DUPLICATES REMOVED)

=> d l36 1-10 cbib abs

L36 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN
2001:923851 Document No. 136:68690 CD154 variants. Hsu, Yen-Ming; Garber, Ellen (Biogen, Inc., USA). PCT Int. Appl. WO 2001096397 A2 20011220, 41 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18517 20010608. PRIORITY: US 2000-PV210657 20000609.
AB Methods of decreasing (e.g., inhibiting) the expression of wild-type CD154 on the surface of a target cell and methods of treating a patient suffering from or predisposed to a CD154-mediated disease. In these methods, a nucleic acid construct that directs expression of a mutant CD154 lacking at least a portion of the tumor necrosis factor homologous domain ("TNFH") is introduced into a target cell (such as a T helper cell or a cytotoxic T cell). The expressed mutant CD154 binds to wild-type CD154 inside the cell, rendering the wild-type protein unable to reach the cell surface.

L36 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1
2000313005 Document Number: 20313005. PubMed ID: 10853016. Establishment of a human colon cancer cell line (PMF-ko14) displaying highly metastatic activity. Okazaki K; Nakayama Y; Shibao K; Hirata K; Sako T; Nagata N; Kuroda Y; Itoh H. (Department of Surgery I, University of Occupational and Environmental Health, Yahatanishi-ku, Kitakyushu 807-8555, Japan.) INTERNATIONAL JOURNAL OF ONCOLOGY, (2000 Jul) 17 (1) 39-45. Journal code: 9306042. ISSN: 1019-6439. Pub. country: Greece. Language: English.
AB A new human colon cancer cell line (PMF-ko14) derived from a peritoneal disseminated tumor has been established and maintained for over 25 months. In tissue culture, the cells grew in a mainly monolayered sheet with a population doubling time of about 27 h. Chromosome counts at the 60th passage ranged from 79 to 84 with a modal number of 83. Flow cytometry of the cell surface **antigen** expression indicated that CD49b, CD29, carcinoembryonic **antigen** (CEA), sialyl Lewis a (sLea), and CD49c were positive in more than 70% of the cells. The nude mouse xenograft models indicated are: subcutaneous or intraperitoneal injection model, **spleen injection**-liver metastasis model, and orthotopic implantation-spontaneous metastasis model. As PMF-ko14 has highly metastatic activity it should prove to be a useful tool for research in biological behavior of metastatic colon cancer.

L36 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 2
1998406360 Document Number: 98406360. PubMed ID: 9733622. Enhancement of

metastatic activity of colon cancer as influenced by expression of cell surface **antigens**. Okazaki K; Nakayama Y; Shibao K; Hirata K; Nagata N; Itoh H. (Department of Surgery I, University of Occupational and Environmental Health, Kitakyushu, 807-8555, Japan.) JOURNAL OF SURGICAL RESEARCH, (1998 Jul 15) 78 (1) 78-84. Journal code: 0376340. ISSN: 0022-4804. Pub. country: United States. Language: English.

AB BACKGROUND: Cell surface **antigens** are contributory factors toward metastatic activity. There have been no detailed studies on changes in cell surface **antigens** of colon cancer cell lines. To control life-threatening metastasis, it is necessary to evaluate what types of changes in cell surface **antigens** exert an influence on metastatic activity. MATERIALS AND METHODS: In vivo selection was performed using the human colon cancer-derived cell line KM12SM to obtain variants of metastatic activity. A murine **spleen injection**-liver metastasis procedure reflecting the latter half of the metastatic process was adopted and repeated four times. Flow cytometric analyses were carried out to detect expression of **antigens**: Lewis a (Lea), Lewis x (Lex), sialyl Lewis a (sLea), sialyl Lewis x (sLex), E-cadherin, CD44v6, integrin alpha2 (CD49b), integrin alpha3 (CD49c), integrin alpha4 (CD49d), integrin alpha5 (CD49e), and integrin beta1 (CD29). RESULTS: In vivo selection produced variants with higher metastatic activity. In the original line KM12SM, sLea, E-cadherin, CD49b, CD49c, or CD29 were positive in more than 40% of the cells. After selection, the percentage of cells positive for Lea, sLea, and all examined integrins significantly increased. Lex, sLex, and CD44v6 increased slightly, while E-cadherin decreased slightly. CONCLUSIONS: In vivo selection and flow cytometric analysis revealed that Lea, sLea, CD49b, CD49c, and CD29 appear to be involved in the increase of metastatic activity. The changes of integrin expression in this study suggest that integrins collaborate in the promotion of adhesion to an extracellular matrix.

L36 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN

1997:577695 Document No. 127:292002 Donor-specific toxic cell's (donor spleen cells loaded with ricin) effect on inducing tolerance to skin allografts in mice. Wang, Chongqing; Guan, Yinghui; Li, Qijing (Coll. Life Sci., Beijing Univ., Beijing, 100871, Peop. Rep. China). Beijing Daxue Xuebao, Ziran Kexueban, 33(2), 230-239 (Chinese) 1997. CODEN: PCTHAP. ISSN: 0479-8023. Publisher: Beijing Daxue Chubanshe.

AB A new approach for preventing rejection of allografts is described. The skin allograft donors were C57BL/6 mice and the recipients were BALB/C mice. Calcium chloride was used to transfect ricin into donor spleen cells, which was tail-vein injected into recipient blood. There were two test groups, and they were all injected with toxic cells after or before skin transplantation. The survival time of skin allografts in both test groups was prolonged compared with control groups. The results of statistical tests (t-test) also verified that the difference between each pair of test and control groups was very significant ($t > t0.01$). The immune response to donor major histocompatible **antigen** complex of both test groups were suppressed.

L36 ANSWER 5 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 3

97120999 EMBASE Document No.: 1997120999. Protection of mice against visceral leishmaniasis by immunization with promastigote **antigen** incorporated in liposomes. Ali N.; Afrin F.. N. Ali, Leishmania Group, Indian Institute of Chemical Biology, 4 Raja S. C. Mullick Road, Calcutta 700 032, India. Journal of Parasitology 83/1 (70-75) 1997. Refs: 52.
ISSN: 0022-3395. CODEN: JOPAA2. Pub. Country: United States. Language: English. Summary Language: English.

AB Leishmanial **antigens** (LAg) were used as a vaccine against Leishmania donovani, the causative agent of visceral leishmaniasis. BALB/c mice, immunized intraperitoneally with 20 .mu.g of the **antigen**

in phosphate-buffered saline (PBS) or entrapped in liposomes, were infected intravenously with 2 X 107 L. donovani promastigotes. Mice immunized with PBS and empty liposomes showed similar levels of parasite burdens in the liver and **spleen**. **Injection** of the **antigen** alone or entrapped in liposomes, followed with infection, induced significant levels of protection against the disease. After 2 and 4 mo of infection, mice immunized with free **antigen** induced 7.4% and 50.7% reduction in the liver parasite burden, respectively, compared to control (PBS) mice. With **antigen** encapsulated in liposome, the liver parasite burden was further reduced by 30.4% and 73% at 2 and 4 mo by infection, respectively. Splenic parasite burden was very low at 2 mo of infection. At 4 mo, the parasite level was reduced by 54.2% with free **antigen** and 69.3% with **antigen** entrapped in liposomes. Whereas the protection induced by the free **antigen** is mainly cell mediated, stimulation of an antibody response together with a strong delayed-type hypersensitivity may be responsible for the better protection with liposomal **antigen**.

L36 ANSWER 6 OF 10 EMBASE
on STN

91337441 EMBASE Document No.: 1991337441. Effects of castration, Depo-testosterone and cyproterone acetate on lymphocyte T subsets in mouse thymus and spleen. Aboudkhil S.; Bureau J.P.; Garrelly L.; Vago P.. Lab. Cell Biol./Immunogenetics, Faculty of Medicine, Av. Kennedy 3000,Nimes, France. Scandinavian Journal of Immunology 34/5 (647-653) 1991. ISSN: 0300-9475. CODEN: SJIMAX. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The effects of testosterone on the relative proportion of Thy 1.2, Cd4 (L3T4) and CD8 (Lyt-2) cells in thymus and spleen were studied after castration and administration of Depo-testosterone (DT) separately or together with cyproterone acetate (CA) (an antiandrogen) in BDF1 mice. Injection of 0.5 mg/100 g body weight of DT during 2 weeks decreased significantly the number and proportion of double positive (DP) (CD4+ CD8+) and increased the percentage of single positive (SP) CD4+ (CD4+ CD8-), whereas there was a slight decrease in the Thy 1.2 + cells in the thymus. In parallel, we observed an increase in CD8+ (CD4- Cd8+) cells in the spleen. The androgen deprivation after 3 weeks of castration induced a decrease in the percentage of CD4+ cells in thymus and both CD4+ and CD8+ cells in **spleen**. **Injection** of CA (0.5 mg/100 g body weight) had the same qualitative effects as DT on the proportion of lymphocyte T subsets in castrated mice. However, the combined activities of DT and CA were greater than either alone. These data indicate the main role of testosterone in the distribution of CD4+ and CD8+ cells in male mice. The similar effects of CA and DT in the lymphoid organs may suggest a difference between androgen receptors of sexual and lymphoid organs.

L36 ANSWER 7 OF 10 EMBASE
on STN

81128893 EMBASE Document No.: 1981128893. Immmunogenetic differences between lymph node cell and bone marrow cell grafts in irradiated mice. Eastcott J.W.; Broitman S.A.; Bennett M.. Dept. Microbiol., Boston Univ. Sch. Med., Boston, Mass. 02118, United States. Cellular Immunology 59/2 (378-391) 1981.
CODEN: CLIMB8. Pub. Country: United States. Language: English.

AB C3H lymph node cell (LNC) grafts, but no bone marrow cell (BMC) grafts, were resisted by lethally irradiated NZB, (C57BL x NZB)F1, and (C57BL/6 x DBA/2)F1 mice. BALB/c hosts did not resist C3H LNC, suggesting that Ir-like genes regulate resistance to such grafts. Cyclophosphamide, silica particles, and 89Sr pretreatments of prospective host mice resulted in successful proliferation of C3H LNC in most instances. These agents were known to abrogate resistance to incompatible BMC grafts. The determinants for **antigens** recognized on LNC appear to map in or near the D region of H-2. LNC grafts of all H-2(k) strains tested (C3H, CBA, C58, C57BR) were strongly resisted while A, C3H.A, B10.A(5R), A.TL, and A.Tla(b) LNC grafts were not strongly resisted by NZB hosts. Grafts of

H-2(b) (C57BL/6, C57BL/10,129) LNC, or BMC are resisted by NZB or (C57BL/6 x DBA/2)F1 hosts. (C3H x C57BL)F1 LNC but not BMC were resisted by similar hosts. (C57BL/6 x DBA/2)F1 mice were injected with C57BL/6 spleen cells four times to induce specific ''unresponsiveness'' to parental-strain Hemopoietic histocompatibility (Hh) **antigens**. Unresponsiveness was induced to C57BL/6 BMC, as expected, but C57BL/6 and C3H LNC grafts were resisted despite the **spleen injections**. The data suggest that the **antigens** recognized during rejection of C3H LNC are not expressed on C3H BMC. It is even conceivable that Hh **antigens** on C57BL/6 BMC and LNC have separate determinants. Alternatively, the injections of C57BL/6 spleen cells may have induced an anti-idiotypic response that was capable of eliminating C57BL/6 LNC by a different effector mechanism.

L36 ANSWER 8 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 4

79108442 EMBASE Document No.: 1979108442. Development of immunosuppressor cells. Umiel T.; Globerson A.; Trainin N.. Dept. Biol., Weizmann Inst. Sci., Rehovot, Israel. Transplantation 24/4 (282-289) 1977. CODEN: TRPLAU. Pub. Country: United States. Language: English.

AB The suppressive activity of neonatal liver cells was studied using in vitro and in vivo experimental models of cell-mediated immunity. Native liver cells could exert a nonstrain-specific suppressive effect, as measured in vitro in the mixed lymphocyte culture reaction. In the in vivo system, which consisted of the assay of mortality of sublethally irradiated (C3H/eb x C57BL/6)F1 mice challenged with parental C57BL spleen cells, the mice died within 100 days of **spleen injection**. However, when the spleen cells were injected in a mixture with parental (C57BL) liver cells, there was no mortality. Prevention of graft-versus-host response by liver cells was strain specific and was manifested only in systems where spleen cells were syngeneic to the liver cells used, but not when spleen and liver cells were unrelated. The suppressive effect of the liver in vivo was found to depend on thymic function, since no suppression of graft-versus-host response by liver cells could be detected in thymectomized irradiated hosts. Preincubation of these liver cells with thymic hormone, before administration to the thymectomized hosts in a mixture with spleen cells, led to manifestation of the suppressive capacity. Thus, suppressor cells seem to be present in the neonatal liver, and they subsequently undergo an additional phase of maturation that enables their further maintenance in vivo and the specific expression of their suppressive function in the irradiated recipient. Simultaneously, it is suggested that presence of **antigen** and thymic function may be critical in directing the pattern of differentiation of liver-specific suppressors.

L36 ANSWER 9 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 5

76116002 EMBASE Document No.: 1976116002. Nonspecific elicitation of antibody forming cells in the mouse spleen by bacterial lipopolysaccharide. Nakano M.; Uchiyama T.; Tanabe M.J.; Saito K.. Dept. Microbiol., Jichi Med. Sch., Yakushiji, Japan. Japanese Journal of Microbiology 19/2 (141-148) 1975. CODEN: JJMBAN. Language: English.

AB Mechanisms of nonspecific elicitation of anti sheep erythrocyte (SRBC) hemolytic antibody plaque forming cells (PFC) in mouse spleens with an injection of bacterial endotoxin (lipopolysaccharide (LPS)) were studied in comparison with the genesis of naturally occurring 'background' PFC in normal mouse spleens and of rapidly arising PFC in mouse spleens after immunization with SRBC. The cytokinetic pattern of anti SRBC PFC response after an injection of LPS was quite different from that of the response elicited after immunization with SRBC. In addition, even though LPS nonspecifically elicited anti SRBC PFC response in mice, LPS could not confer any immunological memory on mouse immunocytes for a 'secondary type' anti SRBC PFC response to restimulation with LPS or SRBC. The administration of rabbit anti mouse thymocyte immunoglobulin or anti SRBC antiserum in mice markedly suppressed the PFC response after immunization